

# Rheumatoid Arthritis Instances that have RANKL (Receptor Activator of Nuclear Factor Kappa Ligand) Methylation

## Abstract

### Background

Rheumatoid arthritis (RA) is an autoimmune seditious complaint characterized by sinusitis, cartilage damage and bone resorption. Methylation of deoxyribonucleic acid plays a pivotal part in repressing gene expression. Receptor activator of nuclear factor- kappa ligand (RANKL) controls bone homeostasis.

Aim of the work

To assess the serum position of RANKL and its gene protagonist methylation in RA cases and to determine its association with clinical characteristics and complaint exertion.

### Cases and styles

The study included 40 RA cases and 40 controls. The complaint exertion score (DAS28) was assessed. Frequence of RANKL gene protagonist methylation was determined by quantitative methylation specific PCR (QMSP) and serum RANKL position by enzyme linked immunosorbent assay (ELISA).

### Results

Cases mean age was  $46.8 \pm 10.6$  times, 36 ladies and 4 males (F M 91) with median complaint duration 4.5 times. Positive rheumatoid factor, anti-cyclic citrullinated peptide and C- reactive protein were present in 65, 75 and 55 of cases. Methylation chance of RANKL gene protagonist was significantly lower in cases (3.4) than in controls (3.7) ( $p = 0.035$ ) while serum position was significantly increased in cases (9.1 ng/ ml, 5.3 – 11.8 ng/ ml) than in controls (5.7 ng/ ml, 4.5 – 8 ng/ ml) ( $p = 0.003$ ). RANKL methylation frequence was equally associated with serum position ( $r_s = -0.21$ ,  $p = 0.06$ ). There was no significant correlation of RANKL serum position and methylation with DAS28 ( $r = 0.03$ ,  $p = 0.87$  and  $r = 0.06$ ,  $p = 0.73$  independently). RANKL serum position ( $>9.5$  ng/ ml) and methylation chance ( $\leq 9$ ) significantly distinguish RA cases from control (perceptivity 47.5, particularity 91.9;  $p = 0.001$  and perceptivity 100, particularity 40;  $p = 0.03$  independently).

### Conclusion

RA cases expressed elevated serum RANKL with low methylation.

**Keywords:** Rheumatoid arthritis • Methylation • RANKL • Gene protagonist • DAS28

### Introduction

Rheumatoid arthritis (RA) is an autoimmune seditious complaint characterized by synovitis, cartilage destruction, bone corrosion and impairment of the quality of life. The global frequence of RA is ranging from 0.24 to 1.

Multiple factors affect the prevalence of RA as age, coitus, race, smoking history, and civic living. The exact cause of RA is unknown yet; both inheritable and environmental factors contribute to RA pathogenesis. The diapason of RA phenotype in Egypt is variable across

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the country with an adding shift in the F M rate. The age at onset was lower than in other countries. Epigenetics is defined as changing the gene expression without changing the sequence of DNA. It includes methylation of DNA, variations of histones and micro-RNAs. It plays an important part in cell isolation and growth. Epigenetic changes contribute too numerous conditions as cancer and autoimmune conditions. DNA methylation plays a central part in silencing genes. The mortal Receptor activator of nuclear factor kappa ligand (RANKL) gene is located on chromosome. It's expressed by numerous cells similar as osteoblasts, fibroblasts, and T cells. RANKL binds to its receptor on preosteoclasts and activates osteoclasts leading to resorption of the bone. RANKL has a crucial part in numerous natural processes similar as, bone homeostasis, impunity and inflammation. RANKL is an important middleman of bone resorption in RA, is intertwined in colourful osteoimmunological conditions and plays an important part in cancer by enhancing osteolysis and easing bone metastasis [1, 2].

To the stylish of our knowledge, this is a commanding study on the frequence of the methylation position of RANKL gene in Egyptian RA cases. The end of the present work was to assess the serum position of RANKL and the methylation of its gene protagonist in RA cases and determine the association to clinical characteristics and complaint exertion.

### Cases and Methods

This work included 40 RA cases diagnosed according to the 2010 American council of rheumatology/ European league against rheumatism (ACR- EULAR) criteria (19) signed from the Rheumatology Department clinic at Mansoura University Hospitals as well as 40 age and coitus matched control. Cases with other autoimmune complaint, seditious complaint, severe infections, systemic diseases and cancer were barred. The study was approved by the Institutional Review Board (IRB) ethical commission, Faculty of Medicine, Mansoura University (MDP.19.11.34). Cases handed their informed concurrence to share [3].

Detailed history taking and thorough clinical evaluation with special consideration on complaint duration, duration of morning stiffness (MS), tender joint count (TJC), blown common count (SJC) and current specifics. Serum erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), anti-cyclic-citrullinated peptide (anti-CCP) and rheumatoid factor (RF) were attained from the medical records. The complaint exertion score (DAS- 28) was assessed and cases distributed according

to the exertion grades into absolution, low, moderate and high [4].

### Discussion

Rheumatoid arthritis is considered the most common autoimmune seditious arthropathy that can affect in common damage. DNA methylation affects the expression of genes and mokes in the pathogenesis of conditions. Lately, utmost of the experimenters studying DNA methylation have concentrated on protagonist regions of the genes which are important in transcriptional regulation of genes. It has lately been demonstrated that osteoclasts are responsible for bone destruction in RA. RANKL, an osteoclast isolation factor, belongs to the excrescence necrosis factor superfamily and plays a critical part in osteoclast isolation. RANKL is largely expressed in the synovial apkins in cases with RA and is involved in osteoclast development and therefore bone destruction. In the current study, the methylation chance of RANKL gene protagonist was significantly lower in RA cases compared to controls. Reported that proinflammatory cytokines affect the expression of DNA methyl transferases and function in RA. In the current study, there was a no significant correlation between the methylation chance of RANKL gene protagonist and complaint exertion [5, 6].

In the present work, the serum RANKL position was significantly advanced in RA cases compared to controls this coincides with that of others. Bruno etal. Reported that seditious cytokines increase the product of RANKL. The increased position of RANKL stimulates osteoclast performing in bone resorption which is a crucial point of RA. This may explain the part of RANKL in the pathogenesis of RA. In this work, there was no significant correlation between serum RANKL position and complaint exertion. Couldn't find any association of RANKL with complaint exertion while lately others set up a relation. In a study on Syrian RA cases it was reported that elevated serum RANKL can be used as an index of complaint exertion and a new individual biomarker in cases with early complaint. This distinction may be explained by different age range, inflexibility and duration of complaint [7, 8].

In the current study, there was no significant difference in the methylation chance of RANKL protagonist and age of cases. In harmony. Showed that only 2 of the CpG spots of genome change with age. It has been reported that long duration exposure to cytokine can affect the DNA methylation pattern. Consequently, the current work assessed the association between methylation chance of RANKL gene protagonist and DAS- 28

with no significant relation. Likewise, the current study revealed no correlation between serum RANKL position and DAS- 28. Still, others reported a significant correlation.

Presently, there was an inverse relation between serum RANKL position and age of cases in agreement to former studies. Likewise, the current study revealed a negative association between serum RANKL position and complaint duration. In disagreement, others showed that serum RANKL position increases with complaint duration in RA.

In the present work, methylation chance of RANKL

gene protagonist showed no significant association with either CRP or RF. still, serum RANKL position tended to be advanced in cases with a positive RF. Smolen et al. Reported that RF seropositivity is a poor prognostic marker of RA. Also, in this study serum RANKL position tended to be advanced in CRP positive cases and this agrees with former studies [9, 10].

**Conflict of Interest**

None

**Acknowledgment**

None

**References**

1. Xunrong L, Yan AW, Liang R *et al.* Hepatitis B virus (HBV) reactivation after cytotoxic or immunosuppressive therapy--pathogenesis and management. *Rev Med Virol.* 11, 287-99 (2001).
2. Ekpanyapong S, Reddy KR. Hepatitis B Virus Reactivation: What Is the Issue, and How Should It Be Managed? *Clin Liver Dis.* 24, 317-333(2020).
3. Huang SC, Yang HC, Kao JH *et al.* Hepatitis B reactivation: diagnosis and management. *Expert Rev Gastroenterol Hepatol.* 14, 565-578 (2020).
4. Reddy KR, Beavers KL, Hammond SP *et al.* American Gastroenterological Association Institute guideline on the prevention and treatment of hepatitis B virus reactivation during immunosuppressive drug therapy. *Gastroenterology.* 148: 215-219 (2015).
5. Su YC, Lin PC, Yu HC *et al.* Hepatitis B virus reactivation in patients with resolved hepatitis B virus infection receiving chemotherapy or immunosuppressive therapy. *Eur J Gastroenterol Hepatol.* 30, 925-929 (2018).
6. Pisaturo M, Di Caprio G, Calò F *et al.* Management of HBV reactivation in non-oncological patients. *Expert Rev Anti Infect Ther.* 16(8), 611-624 (2018).
7. Law MF, Ho R, Cheung CK *et al.* Prevention and management of hepatitis B virus reactivation in patients with hematological malignancies treated with anticancer therapy. *World J Gastroenterol.* 22(28), 6484-500 (2016).
8. Shibolet O, Ilan Y, Gillis S *et al.* Lamivudine therapy for prevention of immunosuppressive-induced hepatitis B virus reactivation in hepatitis B surface antigen carriers. *Blood.* 100, 391-396 (2002).
9. Sagnelli C, Pisaturo M, Calò F *et al.* Reactivation of hepatitis B virus infection in patients with hemolymphoproliferative diseases, and its prevention. *World J Gastroenterol.* 25, 3299-3312 (2019).
10. Manzano-Alonso ML, Castellano-Tortajada G. Reactivation of hepatitis B virus infection after cytotoxic chemotherapy or immunosuppressive therapy. *World J Gastroenterol.* 17, 1531-1537(2011).